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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,547	06/28/2001	William R. Wagner	214001-00810-1	6231

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
07/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/894,547	WAGNER ET AL.	
	Examiner	Art Unit	
	Ileana Popa	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-19,29-32 and 2127* is/are pending in the application.

4a) Of the above claim(s) *6,14-18,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 7-13, 19, 23-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

2. Claims 4, 20, and 28 have been cancelled. Claims 6, 14-18, 21, and 22 have been withdrawn. Claims 1-3, 11, and 29 have been amended. Claims 30-32 are new.

Claims 1-3, 5, 7-13, 19, 23-32 are under examination.

Response to Arguments

Claim Objections

3. The objection to claim 11 objected for containing minor informalities is withdrawn in response to Applicant's amendment to the claim filed on 04/16/2007.

The objection to claim 28 for being in improper dependent form is moot because Applicant cancelled the claim in the response filed on 04/16/2007.

Claim Rejections - 35 USC § 112, second paragraph

4. The rejection to claim 29 under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in response to Applicant's amendment to the claim filed on 04/16/2007.

Claim Rejections - 35 USC § 112 – enablement

5. The rejection of claims 1-3, 5, 7-12, 19, 24, and 26-27 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in response to Applicant's amendment to the claim filed on 04/16/2007.

Claim Rejections - 35 USC § 102

6. The rejection of claims 11 and 12 under 35 U.S.C. 102(b) as being anticipated by Pouletty et al. (U.S. Patent No. 5,612,034) is withdrawn in response to Applicant's argument filed on 04/16/2007. The rejection of claim 28 under 35 U.S.C. 102(b) as being anticipated by Pouletty et al. (U.S. Patent No. 5,612,034) is moot because Applicant cancelled the claim in the response filed on 04/16/2007.

The rejection of claim 11 under 35 U.S.C. 102(e) as being anticipated by Bridon et al. (PGPUB 2002/0018751) is withdrawn in response to Applicant's argument filed on 04/16/2007. The rejection of claim 28 under 35 U.S.C. 102(e) as being anticipated by Bridon et al. (PGPUB 2002/0018751) is moot because Applicant cancelled the claim in the response filed on 04/16/2007.

7. Claims 1, 3, 5, 7, 10, 19, 23, 24, 26, and 29 remain and the new claims 30 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Pouletty et al. (U.S. Patent No. 5,612,034) for the reasons of record set forth in the prior Office action mailed on 03/08/2007. Applicant's arguments filed 04/16/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Pouletty et al. solely discloses introducing a reactive group into the bloodstream to react with circulating blood components, such as blood cells, immunoglobulins and proteins (column 2, lines 41 and 42) in order to provide functionalized blood components for the purpose of increasing their half-life in the bloodstream (column 1, lines 60-62). Applicant submits that nowhere do Pouletty et al. disclose or suggest modifying the surface of vascular tissue to allow the targeted delivery of a chemical or biological entity to the surface of vascular segment. Applicant points out that the disclosure of Pouletty et al. is not directed to targeted delivery at all, but rather to introducing reactive groups into bloodstream components. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

It is noted that the claims recite a method of delivery to a vascular tissue segment, and not a method of targeted delivery to the surface of a vascular tissue segment. It is also noted that the claims do not require delivery to blood vessel segments, wherein blood components were removed by washing. Therefore, the claims encompass systemic delivery and local delivery without blood removal and the claimed method would necessarily result in delivery to all blood components, including endothelial cells, because the claimed delivery system is not cell-specific and in fact the avidin/biotin system would result in delivery to any cell and any protein in the blood. Pouletty et al. teach a method of *in vivo* delivery of agents of interest to blood cells and endothelial cells in patients (i.e., targeted delivery to blood components), wherein the

half-life of the agent of interest is extended (due to the binding to long-lived blood components), and not to introducing reactive groups into the blood components to prolong their half-life, as Applicant argues (Abstract, column 2, lines 1-11). Pouletty et al. clearly teach that endothelial cells are also targeted (column 4, lines 56-65). Therefore, Pouletty et al. anticipate the claimed invention.

7. Claims 1, 3, 5, 7, 10, 13, 19, 23, 24, and 29 remain and the new claims 30 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Bridon et al. (PGPUB 2002/0018751) for the reasons of record set forth in the prior Office action mailed on 03/08/2007. Applicant's arguments filed 04/16/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Bridon et al. solely discloses methods and composition for non-invasive imaging of mammals by using diagnostic agents modified to bind proteins to prolong the half-life of the agents (p. 1, paragraph 0006, p. 2, paragraph 0026). Applicant argues that this is in contrast, which is directed to targeted delivery of chemical or biological entities such as drugs or cells to the surface of the surface of a vascular tissue segment for therapeutic purposes, wherein Bridon et al. disclosure is solely directed to targeting a diagnostic molecule, such as a radioisotope, to the vasculature of an organ for imaging purposes. Applicant argues that Bridon et al. neither teach nor suggest the instant invention as disclosed in claims 1 and 30, that nowhere do Bridon et al. disclose or suggest that the covalent binding of the molecule modifies the surface of a vascular tissue segment so as to allow

for targeted delivery to the surface of the vascular tissue segment. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

With respect to the argument that the instant invention is directed to targeted delivery of chemical or biological entities such as drugs or cells to the surface of the surface of a vascular tissue segment for therapeutic purposes, it is noted that these limitations are not recited in the claims. The claims recite a method of delivery to a vascular tissue segment, and not a method of targeted delivery to the surface of a vascular tissue segment. It is also noted that the claims do not require delivery to blood vessel segments, wherein blood components were removed by washing. Therefore, the claims encompass systemic delivery and local delivery without blood removal and the claimed method would necessarily result in delivery to all blood components, including endothelial cells, because the claimed delivery system is not cell-specific and in fact the avidin/biotin system would result in delivery to any cell and any protein in the blood. Additionally, the claims do not specify what the chemical or biological entity is, nor do they recite a therapeutic purpose. Bridon et al. teach targeted delivery to blood components of a radioisotope, wherein the radioisotope is also delivered to endothelial cells and wherein the covalent binding of the radiosiotope modifies the surface of a vascular tissue segment; the radioisotope of Bridon et al. is a chemical entity that can be used as an imaging agent. Therefore, Bridon et al. anticipate the claimed invention.

Claim Rejections - 35 USC § 103

8. The rejections of claim 28 under 35 U.S.C. 103(a) as being unpatentable over Pouletty et al., in view of both Francis et al. (International Journal of Hematology, 1998, 68: 1-18) and Kaiser et al. (Bioconjugate Chem., 1997, 8: 545-551) and under 35 U.S.C. 103(a) as being unpatentable over Bridon et al., in view of Palasis et al. (U.S. Patent 6,369,039) are moot because Applicant cancelled the claim in the response filed on 04/16/2007. The rejection of claim 11 and under 35 U.S.C. 103(a) as being unpatentable over Bridon et al., in view of Palasis et al. (U.S. Patent 6,369,039) is withdrawn in response to Applicant's argument filed on 04/16/2007.

9. Claims 1-3, 5, 7-12, 19, 24, and 26-27 remain and the new claims 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pouletty et al., in view of both Francis et al. (International Journal of Hematology, 1998, 68: 1-18) and Kaiser et al. (Bioconjugate Chem., 1997, 8: 545-551) for the reasons of record set forth in the prior Office action mailed on 03/08/2007. Applicant's arguments filed 04/16/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Pouletty et al. do not anticipate the claimed invention for the reasons stated above. Applicant argues that Pouletty et al. do not disclose or suggest modifying the surface of a segment of vascular tissue to allow for the targeted delivery of a chemical or biological entity to the surface of the vascular tissue segment and that Francis et al. and Kaiser et al. do not cure this deficiencies of Pouletty et al. Applicant continues arguing that there is no suggestion in

the cited references that would motivate one of skill in the art to combine these teachings and that the Examiner used hindsight in making this rejection. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

Pouletty et al. anticipate the claimed invention for the reasons stated above.

In response to applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The motivation does not have to be explicitly stated in the cited art. The motivation can come from the general knowledge in the art at the time the invention was made. Since the cited art clearly teaches that PEG decrease nonspecific binding, one of skill in the art would have known and been motivated to use PEG when deliver agents to the vascular blood components. Therefore, the instant invention is *prima facie* obvious over the prior art.

10. Claims 1, 3, 5, 7, 10, 13, 19, 23-25, and 29 remain and the new claims 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bridon et al., in view of

Palasis et al. (U.S. Patent 6,369,039) for the reasons of record set forth in the prior Office action mailed on 03/08/2007. Applicant's arguments filed 04/16/2007 have been fully considered but they are not persuasive.

Applicant traversed the instant rejection on the grounds that Bridon et al. do not anticipate the claimed invention for the reasons stated above and that Palasis et al. do not cure the deficiencies of Bridon et al. Applicant argues that there is no suggestion to combine the two references, that one of skill in the art would not have been motivated to do so, and that the Examiner used hindsight in making the rejection. Therefore, Applicant requests the withdrawal of the rejection.

Applicant's arguments are acknowledged, however, the rejection is maintained for the following reasons:

Bridon et al. anticipate the claimed invention for the reasons stated above.

In response to applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The motivation does not have to be explicitly stated in the cited art. The motivation can come from the general knowledge in the art at the time the invention was made. Based on the teachings of the art, one of skill in the art would have known and

been motivated to combine the references in order to obtained a visual display for evaluating the progression of a disease associated with blood and endothelial cell components. Therefore, the instant invention is *prima facie* obvious over the prior art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ileana Popa whose telephone number is 571-272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ileana Popa, PhD

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